

- limited number of different ribonucleic acids and peptides encoded by DNA sequences to be examined,
- (c) screening said transduced cells to see whether some of them have altered a preselected cellular function due to the presence of said ribonucleic acid(s) or said peptide(s) which affect(s) biological functions in the cell, said screening being one which does not require knowledge of 1) chains of mechanisms in the cell, 2) enzymes in the cell, 3) signalling pathways in the cell, or 4) receptors in the cell which generate the preselected cellular function, and
- d) selecting and cloning cells which have altered the preselected cellular function,

wherein the pool of appropriate vectors in step (a) contains synthetic totally random DNA sequences;

and wherein

- (e) the vector DNA in the cells having altered cellular function is isolated and sequenced, and the sequences of the ribonucleic acids or peptides effecting alteration of the preselected cellular function are deduced from the sequenced vector DNA;

and/or

- (f) the ribonucleic acids or peptides effecting alteration of the preselected cellular function are used directly for isolation and identification of a ligand molecule to said ribonucleic acids or peptides.

Claim 9, line 4, after "from" insert --the group consisting of--.

20. (Twice amended) The method according to claim 1, in which the peptide effecting [the phenotypic alteration] alteration in the preselected cellular function also contains a purification tag which enables direct isolation of the peptide as well as of the molecule with which the peptide interacts.

21. (Twice amended) The method according to claim 1, in which appropriate signal peptides, other leader molecules or recognition sequences are also encoded by the vectors in the form of fusion partners to expressed random peptides or to expressed proteins containing random peptide sequences, thereby enabling translocation of [these] the expressed random peptides or the expressed proteins containing random peptide sequences to defined cellular compartments.

Claim 37, line 2, after "from" insert --the group consisting of--.

38. (Amended) The method according to claim [19] 1, wherein the [restrictions consist of the presence of] synthetic random DNA sequences are separated by codons encoding glycosylation sites [or anchor residues].

Add the following new claims:

--69. A method for identification of biologically active ribonucleic acids or peptides or cellular ligands to the biologically active ribonucleic acids or peptides, which comprises the steps of

- (a) producing a pool of appropriate vectors each containing a DNA sequence to be examined,

- (b) efficiently transducing said vectors into a number of identical eukaryotic cells in such a way that each cell expresses either a single ribonucleic acid and possibly peptide encoded by the DNA sequence to be examined or a limited number of different ribonucleic acids and peptides encoded by DNA sequences to be examined,
- (c) screening said transduced cells to see whether some of them have altered a preselected phenotypic trait, wherein the preselected phenotypic trait has been so selected that an observed alteration thereof in a transduced cell provides an indication that said ribonucleic acid(s) or peptide(s) expressed in the transduced cell affects biological function(s) of the transduced cell, where said biological function(s) participate in generating the preselected phenotypic trait, and
- (d) selecting and cloning cells which have altered the preselected phenotypic trait,

wherein the pool of appropriate vectors in step (a) contains synthetic totally random DNA sequences;

and wherein

- (e) the vector DNA in the cells having altered the phenotypic trait is isolated and sequenced, and the sequences of the ribonucleic acids or peptides effecting alteration of the preselected phenotypic trait are deduced from the sequenced vector DNA;

and/or

- (f) the ribonucleic acids or peptides effecting alteration of the preselected phenotypic trait are used directly for isolation and identification of a ligand molecule to said ribonucleic acids or peptides.

70. A method for identification of biologically active ribonucleic acids or peptides or cellular ligands to the biologically active ribonucleic acids or peptides, which comprises the steps of

- (a) producing a pool of appropriate vectors each containing a DNA sequence to be examined, wherein ligation of a DNA fragment into a vector is optimized by performing temperature cycling ligation, thereby maintaining a high diversity of the totally random DNA sequences for transfection into packaging cells,
- (b) efficiently transducing said vectors into a number of identical eukaryotic cells in such a way that each cell expresses either a single ribonucleic acid and possibly peptide encoded by the DNA sequence to be examined or a limited number of different ribonucleic acids and peptides encoded by DNA sequences to be examined,
- (c) screening said transduced cells to see whether some of them have altered a preselected cellular function, said screening being one which does not require knowledge of 1) chains of mechanisms in the cell, 2) enzymes in the cell, 3) signalling pathways in the cell, or 4) receptors in the cell which generate the preselected cellular function, and
- (d) selecting and cloning cells which have altered the preselected cellular function,

wherein the pool of appropriate vectors in step (a) contains synthetic totally random DNA sequences;

and wherein

- (e) the vector DNA in the cells having altered cellular function is isolated and sequenced, and the sequences of the ribonucleic acids or peptides effecting alteration of the preselected cellular function are deduced from the sequenced vector DNA;